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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,096	10/14/2004	Heinz Von der Kammer	P67813US1	6145
136	7590	11/14/2006	EXAMINER	
JACOBSON HOLMAN PLLC 400 SEVENTH STREET N.W. SUITE 600 WASHINGTON, DC 20004			POPA, ILEANA	
			ART UNIT	PAPER NUMBER
			1633	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/511,096

Applicant(s)

VON DER KAMMER ET AL.

Examiner

Ileana Popa

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8/18/06
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 and 16-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 October 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election of the invention of Group IX, drawn to a method of screening for a modulator of neurodegenerative diseases in the reply filed on 08/18/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Since the elected invention of Group IX uses the recombinant non-human animal of the invention of Group VII, the two Groups are rejoined and examined together.

Claims 1-10 and 16-20 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 11-15 are under examination.

Note: Change in Art Unit and SPE

The Examiner of record is now Ileana Popa, Art Unit 1633. Therefore, future correspondence should reflect such changes. Also, at the end of the Action is the information regarding the SPE and the Art Unit.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

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Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 11-15 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or well established utility. Applicant is referred to the utility guidelines published in Federal Register January 5, 2001, Volume 66, Number 5, page 1092-1099.

When determining whether an Applicant has described the utility of the invention, one has to determine whether the Applicant has described a well-established utility. If not, if the Applicant made any assertion to a specific, substantial, and credible utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for use. In contrast to general utility, a specific utility will be specific to the claimed subject matter. A substantial utility defines a real world utility of the invention and utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context use are not substantial utilities (see utility guidelines in Federal Register January 5, 2001, Volume 66, Number 5, pages 1092-1099). For example, both therapeutic method for treatment for a newly discovered or known disease and an assay method for identifying compounds that, themselves, have a "substantial utility" define a "real world" use. Another example is an assay that measure the presence of a material that has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following examples require or constitute further research to identify or confirm a real world use

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and therefore are not substantial utilities: (i) basic research, e.g. studying the properties of the material itself or mechanisms in which the material is involved; (ii) a method of treating an unspecified disease or condition; (iii) a method of assaying for or identifying a material that itself has no specific and /or substantial utility; (iv) a method of making a material that itself has no specific, substantial and credible utility; and (v) a claim to an intermediate for the use in making a final product that has no specific, substantial and credible utility.

A credible utility is a utility that is believable to a person of skill in the art based on the totality of evidence and reasoning provided. Assertions are credible unless (i) the logic underlying the assertion is seriously flawed or (ii) the facts upon which such assertion is based are inconsistent with the logic underlying the assertion. In general, credibility is rarely addressed, but if a person of skill in the art would not accept that the recited disclosed invention is currently available for use, such basis of a utility rejection is proper.

Claim 11 is drawn to a recombinant animal comprising a non-native gene sequence encoding for golgin-245. Claim 13 is drawn to a method of screening for a modulator of neurodegenerative disease by using cells expressing golgin-245 or a fragment, derivative, or a variant thereof. Claims 12, 14 and 15 are drawn to a method of screening for a modulator of neurodegenerative disease by using a recombinant animal that expresses the gene encoding for golgin-245 or a fragment, derivative, or a variant thereof, wherein the recombinant non-human animal is prophetically predisposed to or already has developed symptoms of neurodegenerative disorders.

The instant application discloses recombinant, non-human transgenic animals comprising a non-native gene sequence encoding for golgin-245 or fragments, derivatives or variants thereof (p. 7, paragraph 48) and the use of these animals or of cells expressing golgin-245 or fragments, derivatives or variants thereof in a method of screening for modulators of neurodegenerative diseases, (p. 8, paragraphs 49 and 50). Although it discloses the over-expression of the mRNA encoding for golgin-245 in brain samples taken from patients affected with Alzheimer's disease (p.3, paragraph 13), the specification also teaches that to date there is no experimental data demonstrating a relationship between over-expression of golgin-245 and any neurodegenerative disease (p. 3, paragraph 13). The fact that Applicant found by differential display that golgin-245 is over-expressed in the brain of patients with Alzheimer's disease it is not in itself a proof that golgin-245 participates in the pathology of all neurodegenerative diseases, as claimed or even in the pathology of Alzheimer's disease. The art clearly teaches that the term neurodegenerative disease encompasses distinct diseases that are caused by different genetic factors, other than golgin-245. Mutations of distinct genes such as presenilin and amyloid precursor proteins (Alzheimer's disease), α -synuclein (Parkinson's disease), superoxide dismutase (amyotrophic lateral sclerosis or Lou Gehrig's disease), huntingtin (Huntington's disease) are the cause of distinct neurodegenerative diseases with distinct clinical manifestations (Hardy et al., 1998, Review, Science, 1998, 282: 1075-1079). Applicant makes an assertion that the integrity of intracellular transport is a target for the treatment of several disorders, including neurodegenerative disorders (p. 2, paragraph 12). Although the art teaches

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that a defective axonal transport could be implicated in the pathogenesis of Alzheimer's disease, the art also teaches that the cause for the defective axonal transport is not known and that more research is needed before any conclusion can be drawn. For example, Zhu et al. (TRENDS in Molecular Medicine, 2005, 11: 391-393) teach:

"However, it must be cautioned that the idea, although fascinating, is still controversial because it is still in dispute whether A β is produced and released in the axon, let alone how axonal transport deficits induce increased production of A β . In fact, it was suggested by the same group that A β PP is a kinesin-1 receptor that is transported along with β -site APP-cleaving enzyme (BACE) and presenilin. The concerted action of BACE and presenilin mediates proteolysis of A β PP and produces A β in the same membrane complex along the axon, which suggests that A β can be generated within axonally transported vesicles. However, this work was seriously challenged by another laboratory recently, and more research will be needed before any conclusion can be made."

The specification as filed does not disclose or provide any evidence that points to an activity for golgin-245 and furthermore, there is no art on record that discloses or suggests any activity for the claimed golgin-245. For example, Yoshino et al. (J Cell Sci, 2003, 116: 4441-4454) teach:

"tGolgin-1 (golgin-245, trans golgi p230) and golgin-97 are members of a family of peripheral membrane proteins of unknown function that localize to the trans Golgi network (TGN) through a conservative C-terminal GRIP domain.

In an effort to elucidate effectors regulating TGN biogenesis, we have focused on a group of large peripheral membrane proteins of unknown function characterized by an extensive predicted coiled-coil structure and a conserved C-terminal GRIP domain. The GRIP domain confers localization to the TGN and associated vesicles for all four mammalian GRIP domain-containing proteins (GRIP proteins).

No function has been assigned to any GRIP protein, but indirect evidence support a role in vesicular traffic at the TGN.

We show here that in cells in which GRIP domain-containing fragments from tGolgin-1 or golgin-97 are overexpressed, the structure, resident protein localization and function of the TGN are largely disrupted. The results suggest that GRIP proteins or their ligands function in the maintenance of TGN integrity, probably through regulating TGN membrane protein localization."

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Short et al. (Biochim Biophys Acta, 2005, 1744: 383-395) teach:

"Numerous different proteins are involved in organizing the Golgi apparatus into its typical, stacked, ribbon-like structure. The main player is the Golgi matrix, a complex network of proteins such as the GRASPs, the expanding family of coiled-coil golgins, and their regulatory GTPases of the ARF, ARL, and Rab families.

What is clear is that no single golgin alone can be said to be responsible for maintaining Golgi structure. Rather, it is the complex network of interactions between these proteins that is important."

Given the teachings above it is clear that, although the GRIP domain might function in the maintenance of TGN integrity, this function is not specific for any golgin in particular, since the overexpression of GRIP domains derived from different golgins results in the same effect. Therefore the function of maintaining TGN integrity is not specific for golgin-245.

Applicant contemplates to produce transgenic animals comprising an exogenous golgin-245 and use these animals or cells expressing golgin-245 to screen for modulators of neurodegenerative diseases. As mentioned above, at the time the invention was made and even in the present, there was no function attributed to golgin-245 and the mere fact that golgin-245 is over-expressed in the brain of patients with Alzheimer's disease, as identified by differential display, is not in itself a proof that golgin-245 is related to the pathology of Alzheimer's disease or any other neurodegenerative disorder. Golgin-245 was found, by similar techniques, to be over-expressed in pathological conditions other than neurodegenerative disorders, such as liver tumors induced by hepatocarcinogens (Garcia-Allan et al., J Biochem Mol Toxicol, 2000, 14: 65-72, seep. 68, Table 1). Therefore, golgin-245 over-expression is more likely to be an unspecific event, rather than a disease causative event. Therefore, there

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is no well-established utility for the disclosed produced cells or transgenic animals comprising gogin-245.

The Applicant made an assertion of a specific and substantial utility for the disclosed cells or recombinant non-human animals comprising golgin-245 to identify agents that can modulate neurodegenerative disorders. However, such claimed subject matter is not considered substantial because they require further experimentation to define a "real world" use. Golgin-245 is not known to have any specific activity. Applicant's specification discloses the use of cells and recombinant non-human animals expressing golgin-245 to identify compounds exhibiting an ability to modulate neurodegenerative diseases associated with over-expression of golgin-245. Such is not considered to provide patentably utility because the evidence is that the function of this protein is not known. In effect, because the function of the protein is not known and its correlation with any neurodegenerative disease is not proven, the cells and the recombinant non-human animals and hence, the screening method for a modulator of neurodegenerative disorders, are not of use, as the function of the protein itself is not known and there is no evidence of a phenotype or that the over-expression of gogin-245 is the cause of any neurodegenerative disease. Hence, the specification does not provide a substantial utility for the cells or non-human animals comprising golgin-245, as further experimentation is required to reasonably correlate the over-expression of the gene with any phenotype or neurodegenerative disorder.

Moreover, the specification does not provide any working example disclosing the claimed recombinant non-human animal and therefore the phenotype of the animal (i.e.,

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predisposition to or presenting symptoms of neurodegenerative disease) is only predicted. Therefore, the phenotypes of the recombinant non-human animal comprising golgin-245 and the diseases associated with the phenotypes are not known, therefore the asserted specific and substantial utility lacks credibility. While the specification discloses conventional techniques to obtain the recombinant non-human animal (p. 7, paragraph 48), it does not provide any example of such animals. It would be reasonable to conclude that the utility would not be credible based on the evidence of record. Therefore, for the reasons given above, Applicant's claimed cells and recombinant non-human animal comprising golgin-245 and their use to identify agents that could modulate neurodegenerative disorders are not supported by a substantial and/or credible asserted utility, as further research would be required to reasonably confirm any real world use.

Claim Rejections - 35 USC § 112, 2nd paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

5. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 provides for the use of recombinant, non-human animal for screening, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite

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where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 12 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

6. Claims 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear what Applicants mean by "disorders of one or more substances", wherein the substances are selected from the group consisting of (i) a gene coding for golgin-245, (ii) a transcription product of a gene coding for golgin-245, (iii) a translation product of a gene coding for golgin-245, or (iv) a fragment, a derivative, or variant of (i)-(iii). Do Applicants mean to recite disorders caused by disruption of golgin-245 expression and /or function? Since the metes and bounds of the claims cannot be determined, the claims are indefinite.

7. Claims 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claims 12-15 disclose the broad recitations "neurodegenerative disorders" and the claims also disclose "Alzheimer's disease", which is the narrower statements of the ranges/limitations.

Claim Rejections - 35 USC § 112, written description

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1 "Written Description Requirement" makes it clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosures of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Claims 11-15 are drawn to fragments, derivatives, or variants of golgin-245. As such, claims 11-15 encompass a wide and variable genus of compounds the structure of which is not sufficiently disclosed in the specification and the claims.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude the inventors had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention was "ready for patenting", or by describing

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distinguishing identifying characteristics sufficient to show that the Applicants were in possession of the claimed invention (January 5, 2001, Fed. Reg., Vol. 66, No. 4, pp.1099-11).

In analyzing whether the written description requirement is met for the genus claims, it is determined whether representative numbers of species have been described by their complete structure and functional characteristics.

When the claims are analyzed in light of the specification, the fragment, derivative or variant can be any nucleic acid or polypeptide that can be isolated from nature or be produced by recombinant or synthetic means (p. 3-4, paragraph 14). The genus of fragments, derivatives or variants is very large; and a great deal of variability is encompassed by the instant claims. The instant claims encompass in their breadth any nucleic acid or polypeptide that may or may not be derived from golgin-245. However, with the exception of the nucleic acids of SEQ ID NOs: 3, 5, 7, and 9 encoding for golgin-245 splice variants of SEQ ID NOs: 2, 4, 6, and 8, the specification fails to describe additional representative species of the fragments, derivatives, or variants mentioned above. The specification defines the fragment, derivative, and variant as (i) an alternatively spliced, truncated, or cleaved transcription or translation product, (ii) a mutant, RNA-edited, chemically modified, or otherwise altered translation product, and (iii) any polypeptide derived from golgin-245 in which one or more amino acids are added, deleted or inserted, any shorter or longer polypeptide, or any polypeptide that has at least 80% homology to golgin-245, respectively. Therefore, the fragment, derivative or variant is not particularly limited by its structure. The genus (i.e., the

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fragments, derivatives or variants) is not even described by its function, and the specification does not provide any disclosure as to what would have been the complete structure of sufficient number of species of the claimed genus. Applicants have not provided any information for the functional characterization of the genus. The specification discloses that there are no data correlating golgin-245 to the pathology of the neurodegenerative diseases (p. 3, paragraph 13) and the art does not teach any specific function for golgin-245. The limited characterization provided does not indicate that the Applicants had possession of the claimed genus of fragments, derivatives or variants. Applicants are relying upon the disclosure of four nucleic acids encoding four different splice variants to support an entire genus. Since there is no known function ascribed to them, the fragments derivatives or variants can be derived from golgin-245 or from any unrelated sequence, as long as they have some sequence similarity with golgin-245. For these reasons, taken together with the fact that the specification does not describe a representative number of species by their relevant identifying characteristics, specific features and functional attributes that would distinguish different members of the claimed genus, one of skill in the art would not recognize Applicants to be in possession of the entire genus of fragments, derivatives, or variants. In conclusion, the limited information is not sufficient to reasonably convey to one of ordinary skills in the art that the Applicants were in possession of the instant claimed invention, at the time the application was filed. Thus, it is concluded that the written description requirement is not satisfied for the claimed genus.

Claim Rejections - 35 USC § 112, enablement

10. Claims 11-15 are also rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed inventions are not supported by either a credible asserted utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it will operate as intended without undue experimentation.

11. No claim is allowed.

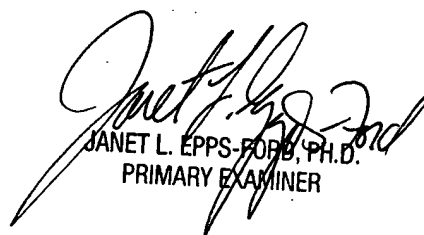
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD



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PRIMARY EXAMINER